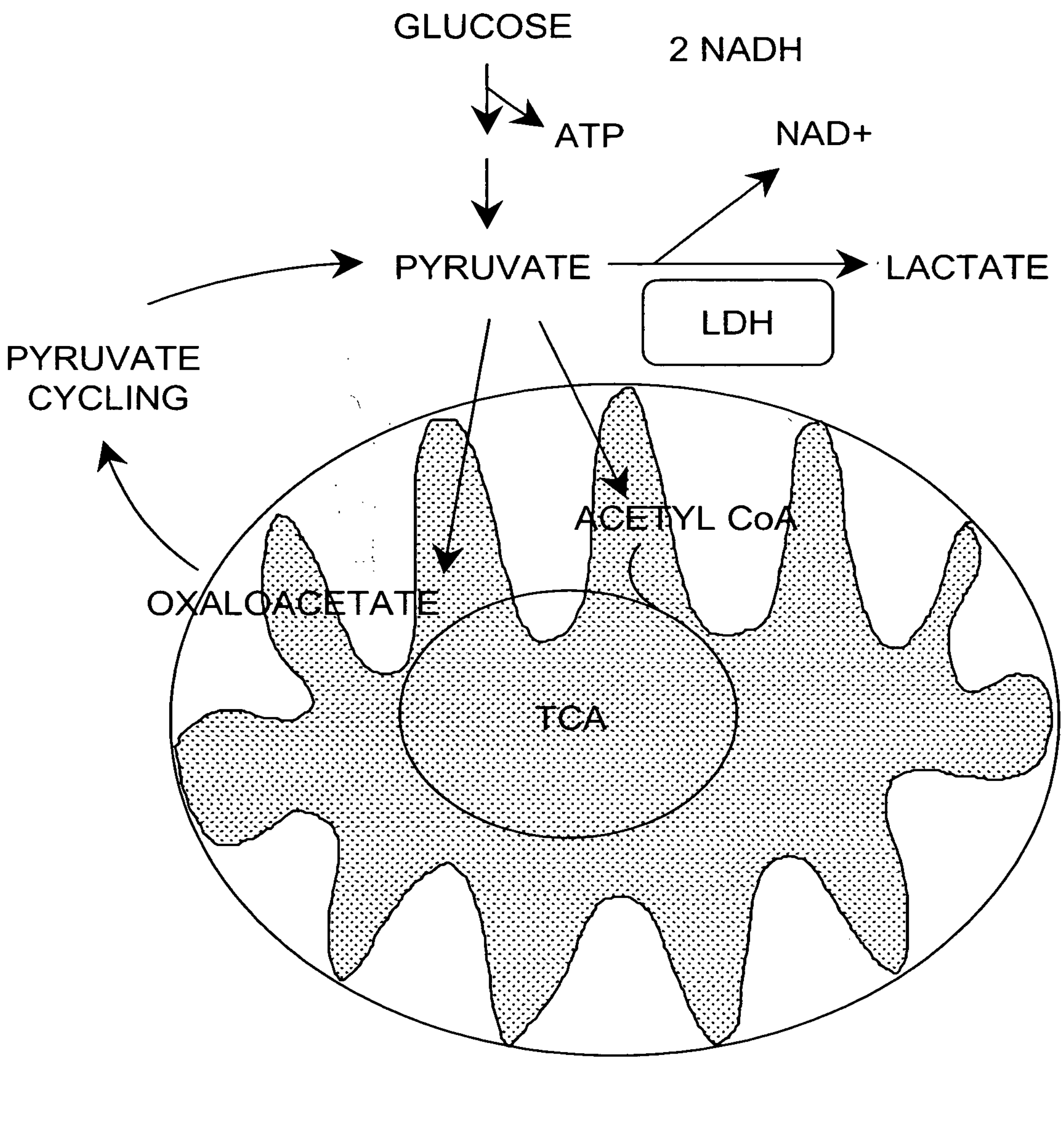

GLUCOSE
2 NADH
ATP
NAD+
PYRUVATE
LACTATE
LDH
PYRUVATE
CYCLING
ACETYL CoA
OXALOACETATE
TCA

FIG. 1

GTGTGCTGGA GCCACTGTCG CCGATCTCGC GCACGCTACT
GCTGCTGCTC GCCCGTCGTC CCCCATCGTG CACTAAGCGG
TCCCAAAAGA TTCAAAGTCC AAG**ATG**GCAG CCCTCAAGGA
CCAGCTGATT GTGAATCTTC TTAAGGAAGA ACAGGTCCCC
CAGAACAAGA TTACAGTTGT TGGGGTTGGT GCTGTTGGCA
TGGCTTGTGC CATCAGTATC TTAATGAAGG ACTTGGCTGA
TGAGCTTGCC CTTGTTGATG TCATAGAAGA TAAGCTAAAG
GGAGAGATGA TGGATCTTCA GCATGGCAGC CTTTTCCTTA
AGACACCAAA AATTGTCTCC AGCAAAGATT ATAGTGTGAC
TGCAAACTCC AAGCTGGTCA TTATCACCGC GGGGGCCCGT
CAGCAAGAGG GAGAGAGCCG GCTCAATTTG GTCCAGCGAA
ACGTGAACAT CTTCAAGTTC ATCATTCCAA ATGTTGTGAA
ATACAGTCCA CAGTGCAAAC TGCTCATCGT CTCAAACCCA
GTGGATATCT TGACCTACGT GGCTTGGAAG ATCAGCGGCT
TCCCCAAAAA CAGAGTTATT GGAAGTGGTT GCAATCTGGA
TTCGGCTCGG TTCCGTTACC TGATGGGAGA AAGGCTGGGA
GTTCATCCAC TGAGCTGTCA CGGGTGGGTC CTGGGAGAGC
ATGGCGACTC CAGTGTGCCT GTGTGGAGTG GTGTGAACGT
CGCCGGCGTC TCCCTGAAGT CTCTGAACCC GCAGCTGGGC
ACGGATGCAG ACAAGGAGCA GTGGAAGGAT GTGCACAAGC
AGGTGGTTGA CAGTGCATAC GAAGTGATCA AGCTGAAAGG
TTACACATCC TGGGCCATTG GCCTCTCCGT GGCAGACTTG
GCCGAGAGCA TAATGAAGAA CCTTAGGCGG GTGCATCCCA
TTTCCACCAT GATTAAGGGT CTCTATGGAA TCAAGGAGGA
TGTCTTCCTC AGCGTCCCAT GTATCCTGGG ACAAAATGGA
ATCTCAGATG TTGTGAAGGT GACACTGACT CCTGACGAGG
AGGCCCGCCT GAAGAAGAGT GCAGATACCC TCTGGGGAAT
CCAGAAGGAG CTGCAGTTC**T** **AA**AGTCTTCC CAGTGTCCTA
GCACTTCACT GTCCAGGCTG CAGCAGGGTT TCTATGGAGA
CCACGCACTT CTCATCTGAG CTGTGGTTAG TCCAGTTGGT
CCAGTTGTGT TGAGGTGGTC TGGGGGAAAT CTCAGTTCCA
CAGCTCTACC CTGCTAAGTG GTACTTGTGT AGTGGTAACC
TGGTTAGTGT GACAATCCCA CTGTCTCCAA GACACACTGC
CAACTGCATG CAGGCTTTGA TTACCCTGTG AGCCTGCTGC
ATTGCTGTGC TACGCACCCT CACCAAACAT GCCTAGGCCA
TGAGTTCCCA GTTAGTTATA AGCTGGCTCC AGTGTGTAAG
TCCATCGTGT ATATCTTGTG CATAAATGTT CTACAGGATA
TTTTCTGTAT TATATGTGTC TGTAGTGTAC ATTGCAATAT
TACGTGAAAT GTAAGATCTG CATATGGATG ATGGAACCAA
CCACTCAAGT GTCATGCCAA GGAAAACACC AAATAAACCT
TGAACAGTG

FIG. 2A

MAALKDQLIVNLLKEEQVPQNKITVVGVGAVGMACAISILMKDLADEL
ALVDVIEDKLKGEMMDLQHGSLFLKTPKIVSSKDYSVTANSKLVIITA
GARQQEGESRLNLVQRNVNIFKFIIPNVVKYSPQCKLLIVSNPVDILT
YVAWKISGFPKNRVIGSGCNLDSARFRYLMGERLGVHPLSCHGWVLGE
HGDSSVPVWSGVNVAGVSLKSLNPQLGTDADKEQWKDVHKQVVDSAYE
VIKLKGYTSWAIGLSVADLAESIMKNLRRVHPISTMIKGLYGIKEDVF
LSVPCILGQNGISDVVKVTLTPDEEARLKKSADTLWGIQKELQF

FIG. 2B

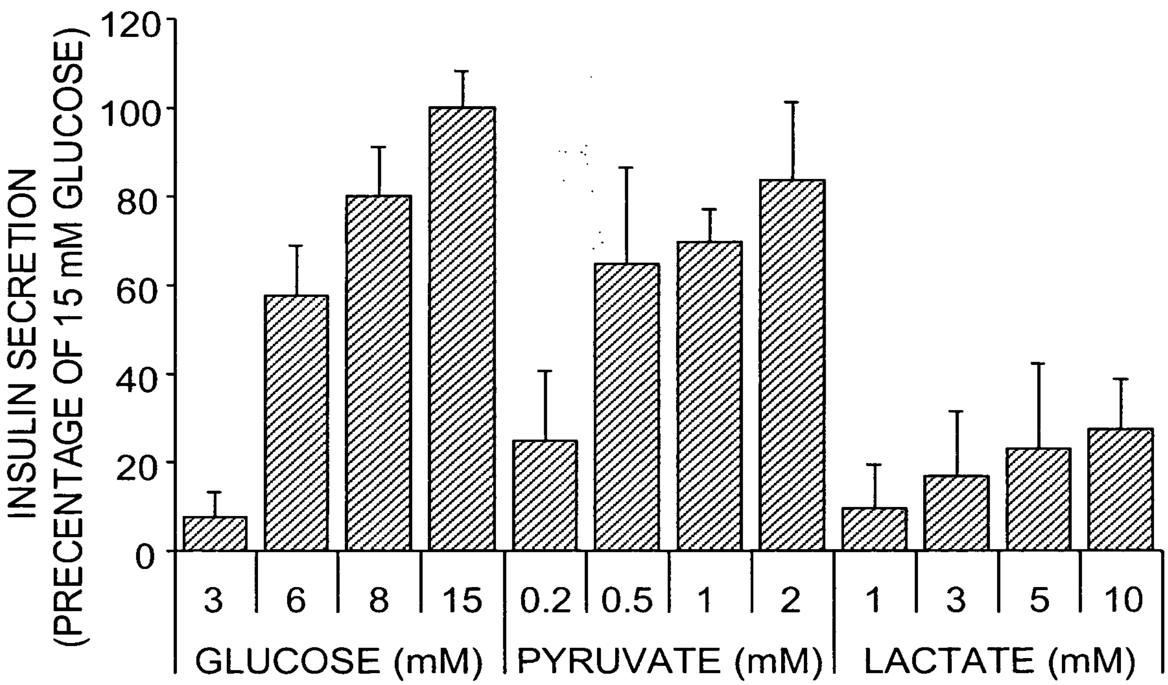
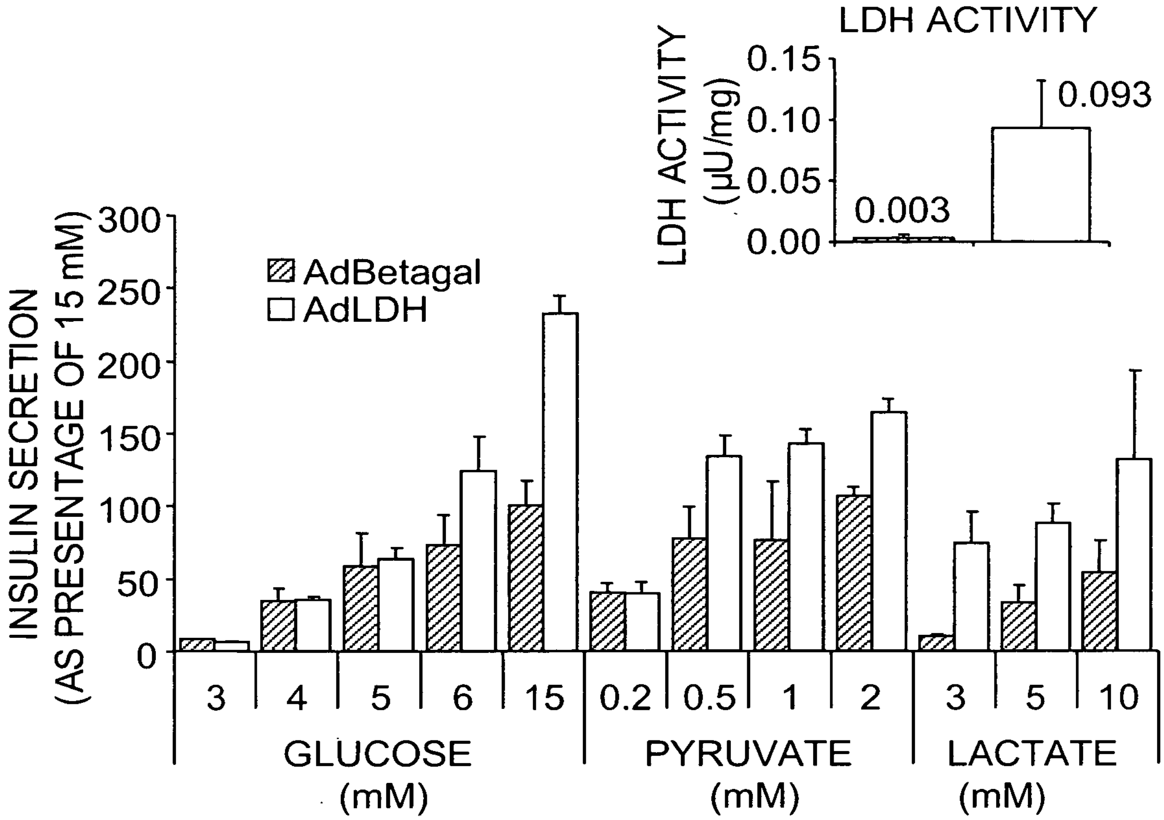
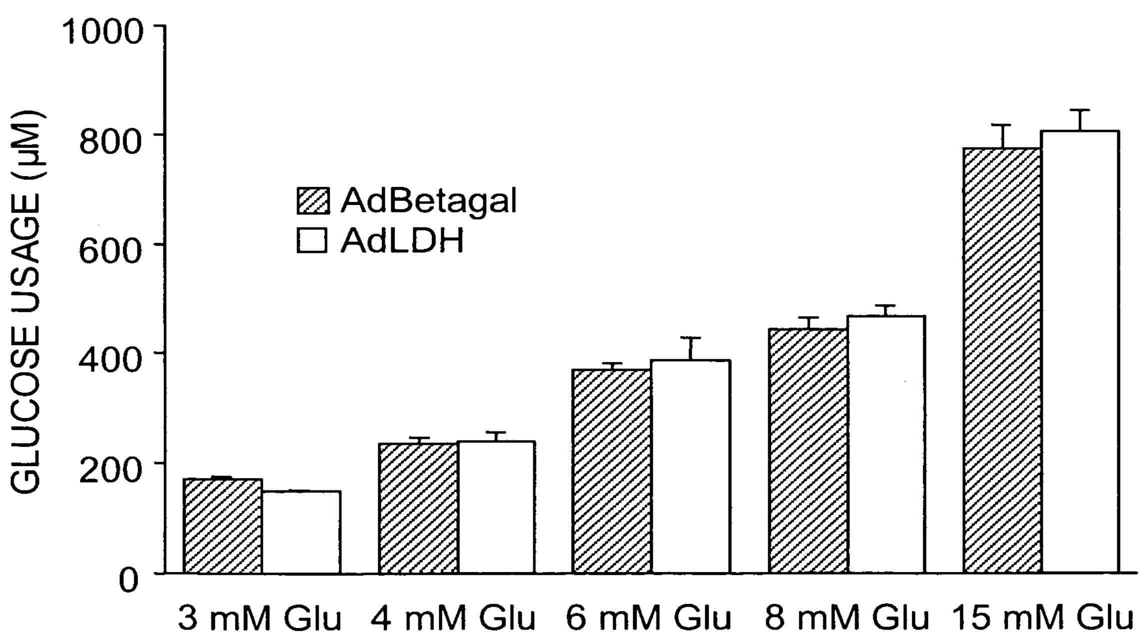


FIG. 3



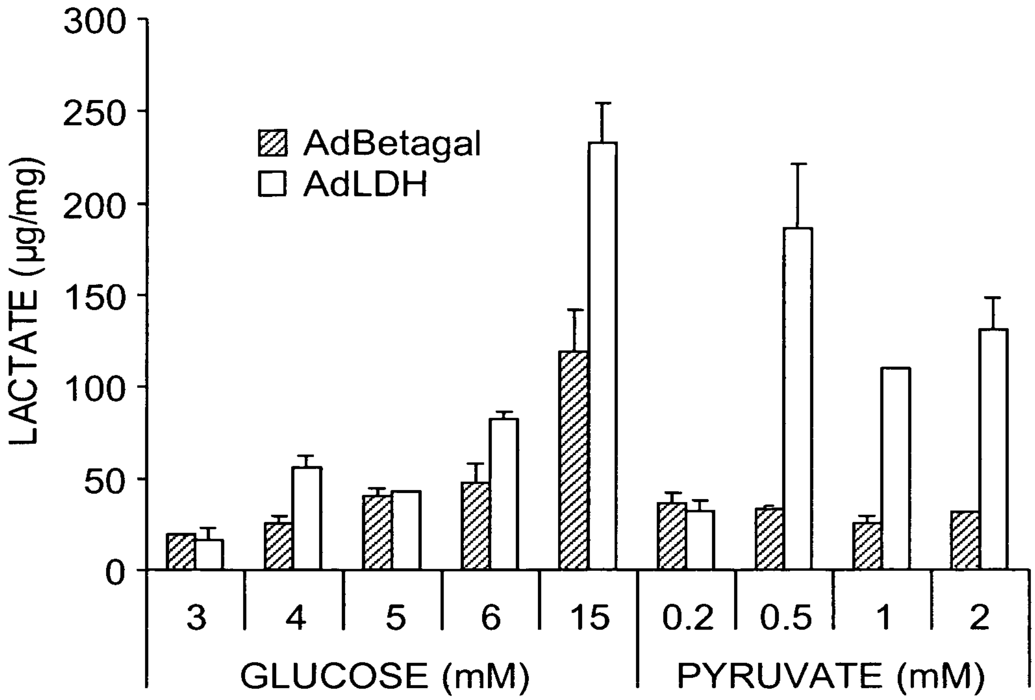
LDH ACTIVITY
LDH ACTIVITY (μU/mg)
0.15
0.10
0.05
0.00
0.003
0.093
INSULIN SECRETION (AS PRESENTAGE OF 15 mM)
300
250
200
150
100
50
0
AdBetagal
AdLDH
3
4
5
6
15
0.2
0.5
1
2
3
5
10
GLUCOSE (mM)
PYRUVATE (mM)
LACTATE (mM)

FIG. 4



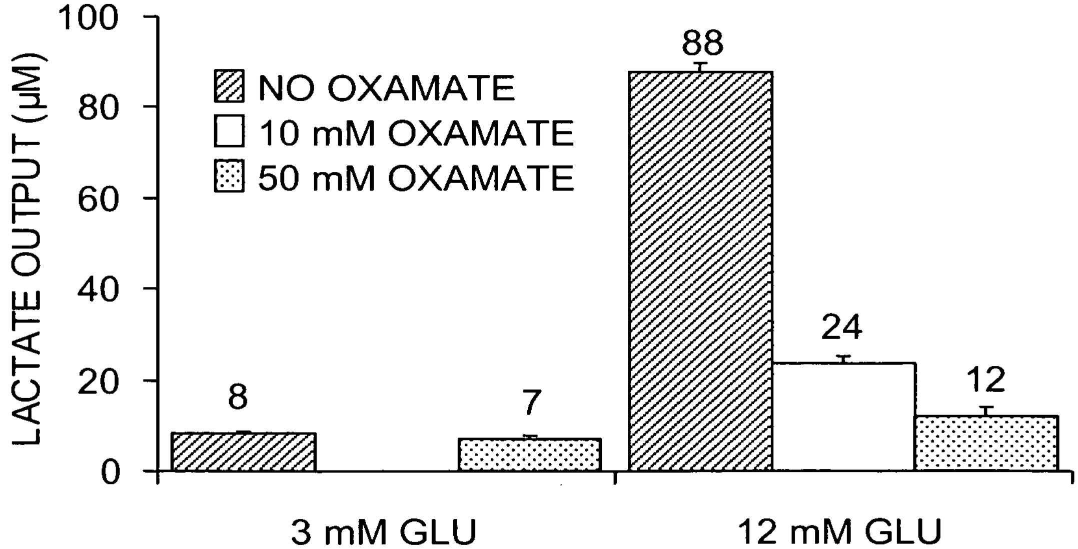
GLUCOSE USAGE (μM)
1000
800
600
400
200
0
AdBetagal
AdLDH
3 mM Glu
4 mM Glu
6 mM Glu
8 mM Glu
15 mM Glu

FIG. 5



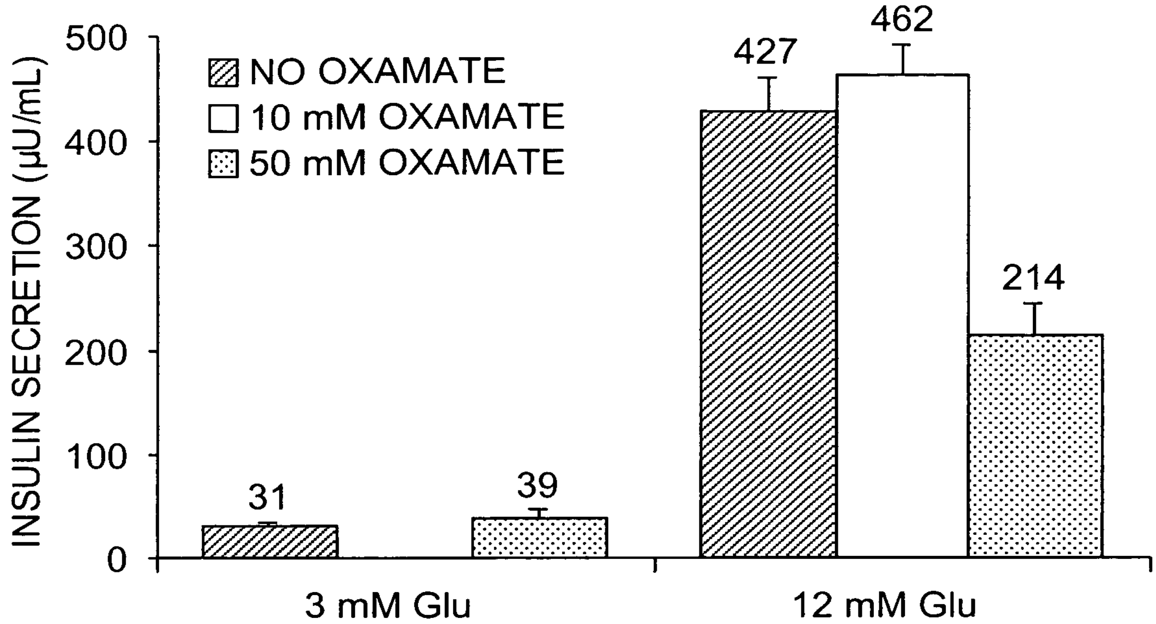
300
250
200
150
100
50
0
LACTATE (µg/mg)
AdBetagal
AdLDH
3
4
5
6
15
0.2
0.5
1
2
GLUCOSE (mM)
PYRUVATE (mM)

FIG. 6



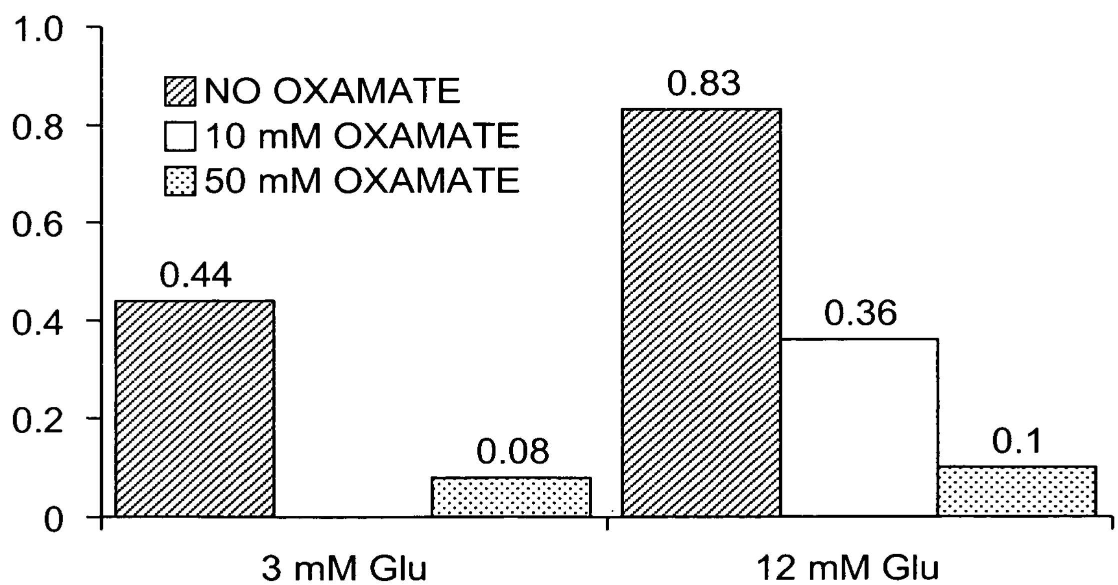
100
80
60
40
20
0
LACTATE OUTPUT (µM)
NO OXAMATE
10 mM OXAMATE
50 mM OXAMATE
88
24
12
8
7
3 mM GLU
12 mM GLU

FIG. 7



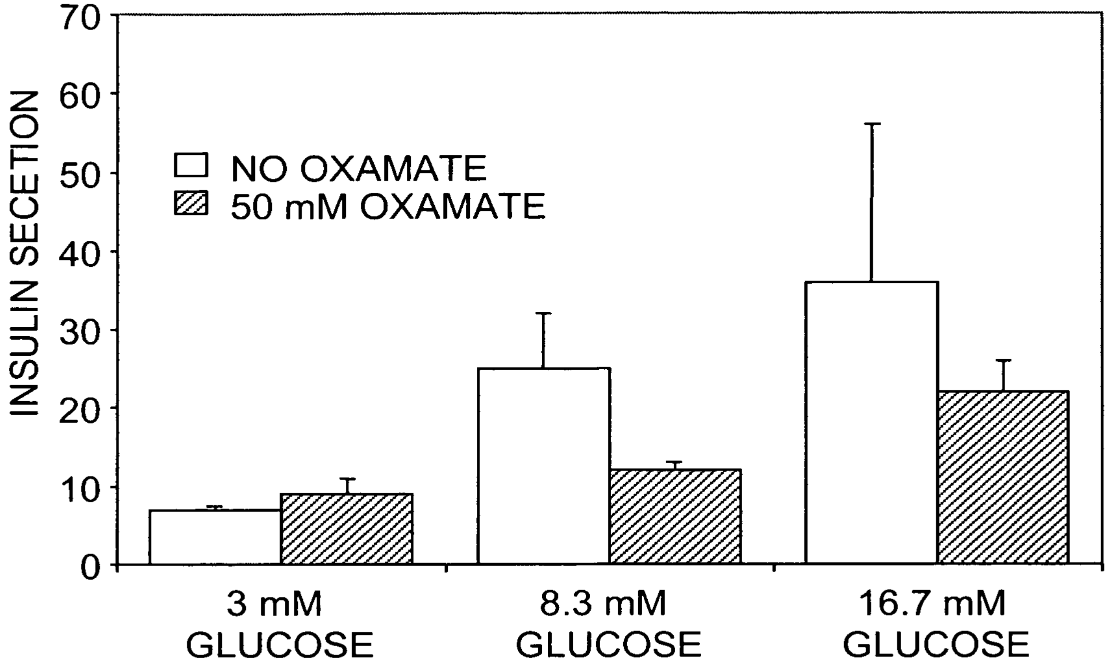
INSULIN SECRETION (μU/mL)
500
400
300
200
100
0
NO OXAMATE
10 mM OXAMATE
50 mM OXAMATE
427
462
214
31
39
3 mM Glu
12 mM Glu

FIG. 7B



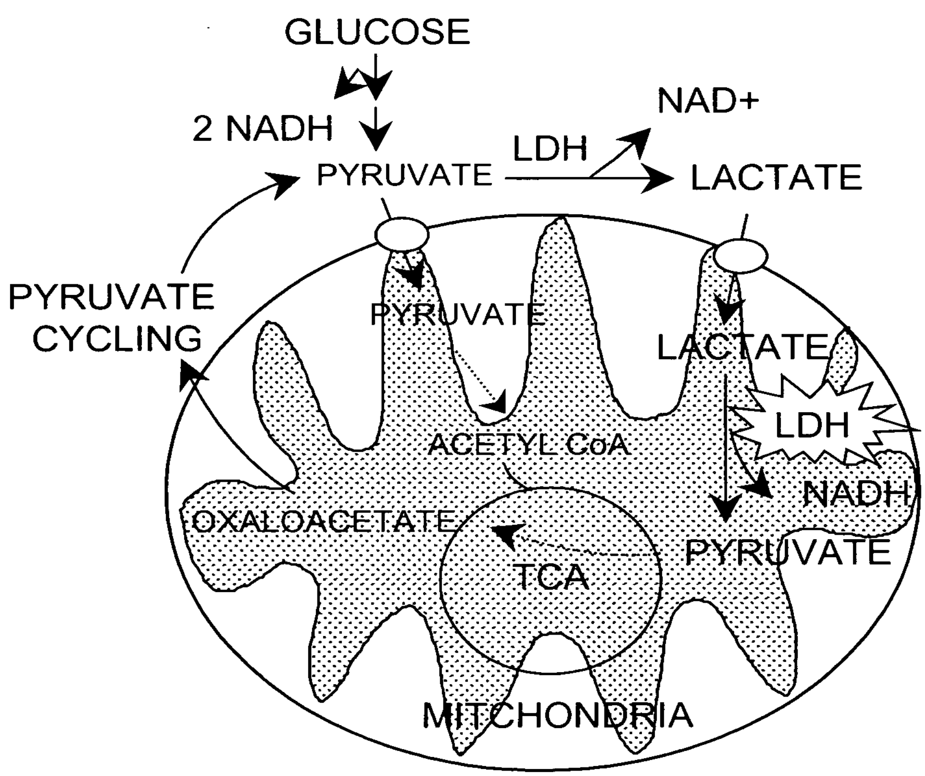
1.0
0.8
0.6
0.4
0.2
0
NO OXAMATE
10 mM OXAMATE
50 mM OXAMATE
0.83
0.44
0.36
0.08
0.1
3 mM Glu
12 mM Glu

FIG. 7C



70
60
50
40
30
20
10
0
INSULIN SECETION
NO OXAMATE
50 mM OXAMATE
3 mM GLUCOSE
8.3 mM GLUCOSE
16.7 mM GLUCOSE

FIG. 7D



GLUCOSE
2 NADH
NAD+
LDH
PYRUVATE
LACTATE
PYRUVATE CYCLING
PYRUVATE
LACTATE
LDH
ACETYL CoA
NADH
OXALOACETATE
PYRUVATE
TCA
MITCHONDRIA

FIG. 8

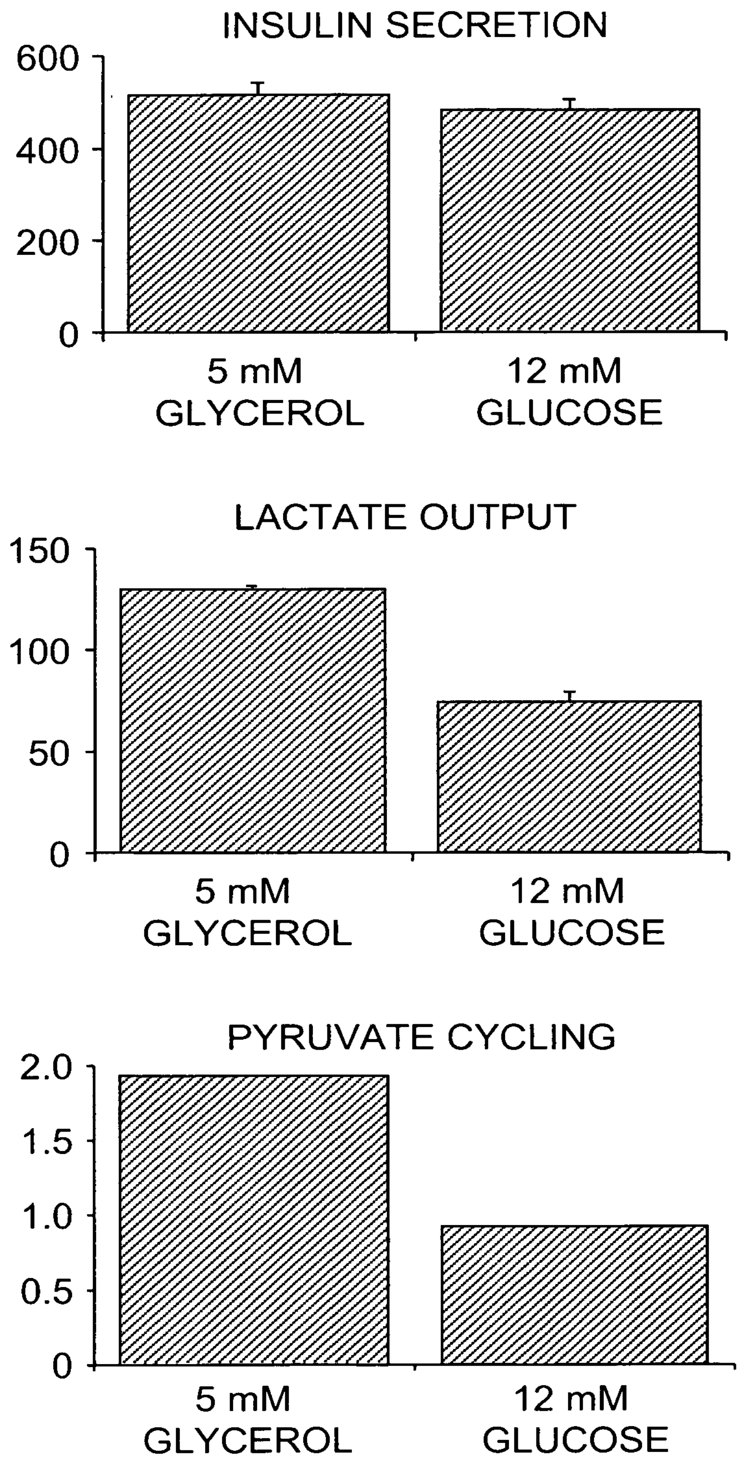

INSULIN SECRETION
600
400
200
0
5 mM
GLYCEROL
12 mM
GLUCOSE
LACTATE OUTPUT
150
100
50
0
5 mM
GLYCEROL
12 mM
GLUCOSE
PYRUVATE CYCLING
2.0
1.5
1.0
0.5
0
5 mM
GLYCEROL
12 mM
GLUCOSE

FIG. 9

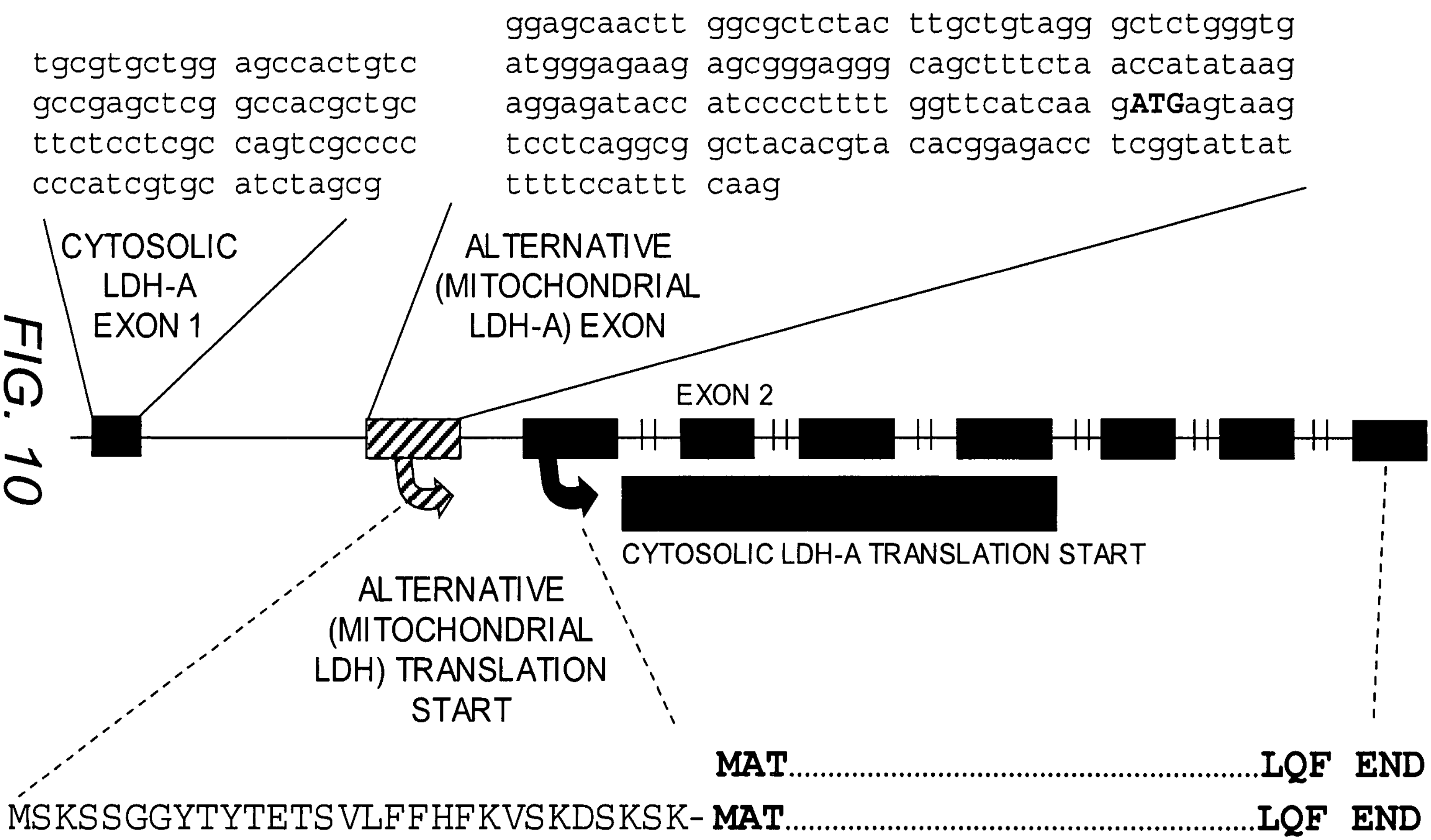

tgcgtgctgg agccactgtc
gccgagctcg gccacgctgc
ttctcctcgc cagtcgcccc
cccatcgtgc atctagcg
ggagcaactt ggcgctctac ttgctgtagg gctctgggtg
atgggagaag agcgggaggg cagctttcta accatataag
aggagatacc atcccctttt ggttcatcaa gATGagtaag
tcctcaggcg gctacacgta cacggagacc tcggtattat
ttttccattt caag
CYTOSOLIC LDH-A EXON 1
ALTERNATIVE (MITOCHONDRIAL LDH-A) EXON
EXON 2
CYTOSOLIC LDH-A TRANSLATION START
ALTERNATIVE (MITOCHONDRIAL LDH) TRANSLATION START
MAT......LQF END
MSKSSGGYTYTETSVLFFHFKVSKDSKSK- MAT......LQF END

FIG. 10

•RAT MSKNSGGYTYTETSVLFFHFKVPKDSKSK
•MOUSE MSKSSGGYTYTETSVLFFHFKVSKDSKSK
•HUMAN MGEPSGGYTYTQTSIFLFHAKIPFGSKSN

•CONS MSK SGGYTYTETSVLFFHFKVPKDSKSK

FIG. 11

```
CGCTCTACTT GCTGTAGGAC TCTGGGTGAT GGGAGAAGAG CGGGAGGGCA
GTTCTTTAAC CGTGTAAGAG GAGGGACCAT CCCTTTTGGG GTTCATCAAG
ATGAGTAAGA ACTCAGGCGG CTACACATAT ACGGAGACCT CAGTATTATT
***
TTTCCATTTC AAGGTCCCAA AAGATTCAAA GTCCAAGATG GCAGCCCTCA
                                        $$$
AGGACCAGCT GATTGTGAAT CTTCTTAAGG AAGAACAGGT CCCCCAGAAC
AAGATTACAG TTGTTGGGGT TGGTGCTGTT GGCATGGCTT GTGCCATCAG
TATCTTAATG AAGGACTTGG CTGATGAGCT TGCCCTTGTT GATGTCATAG
AAGATAAGCT AAAGGGAGAG ATGATGGATC TTCAGCATGG CAGCCTTTTC
CTTAAGACAC CAAAAATTGT CTCCAGCAAA GATTATAGTG TGACTGCAAA
CTCCAAGCTG GTCATTATCA CCGCGGGGGC CCGTCAGCAA GAGGGAGAGA
GCCGGCTCAA TTTGGTCCAG CGAAACGTGA ACATCTTCAA GTTCATCATT
CCAAATGTTG TGAAATACAG TCCACAGTGC AAACTGCTCA TCGTCTCAAA
CCCAGTGGAT ATCTTGACCT ACGTGGCTTG GAAGATCAGC GGCTTCCCCA
AAAACAAAGT TATTGGAAGT GGTTGCAATC TGGATTCGGC TCGGTTCCGT
TACCTGATGG GAGAAAGGCT GGGAGTTCAT CCACTGAGCT GTCACGGGTG
GGTCCTGGGA GAGCATGGCG ACTCCAGTGT GCCTGTGTGG AGTGGTGTGA
ACGTCGCCGG CGTCTCCCTG AAGTCTCTGA ACCCGCAGCT GGGCACGGAT
GCAGACAAGG AGCAGTGGAA GGATGTGCAC AAGCAGGTGG TTGACAGTGC
ATACGAAGTG ATCAAGCTGA AAGGTTACAC ATCCTGGGCC ATTGGCCTCT
CCGTGGCAGA CTTGGCCGAG AGCATAATGA AGAACCTTAG GCGGGTGCAT
CCCATTTCCA CCATGATTAA GGGTCTCTAT GGGATCAAGG AGGATGTCTT
CCTCAGCGTC CCATGTATCC TGGGACAAAA TGGAATCTCA GATGTTGTGA
AGGTGACACT GACTCCTGAC GAGGAGGCCC GCCTGAAGAA GAGTGCAGAT
ACCCTCTGGG GAATCCAGAA GGAGCTGCAG TTCTAAAGTC TTCCCAGTGT
CCTAGCACTT CACTGTCCAG GCTGCAGCAG GGTTTCTATG GAGACCACGC
ACTTCTCATC TGAGCTGTGG TTAGTCCAGT TGGTCCA
```

•* MITOCHONDRIAL START SITE
•$ CYTOSOLIC START SITE
•OVERLINED 5'ORF
•PRIMER SEQUENCES ARE UNDERLINED

FIG. 12A

MSKNSGGYTYTETSVLFFHFKVPKDSKSKMAALKDQLIVNLLKEEQVPQ
NKITVVGVGAVGMACAISILMKDLADELALVDVIEDKLKGEMMDLQHGS
LFLKTPKIVSSKDYSVTANSKLVIITAGARQQEGESRLNLVQRNVNIFK
FIIPNVVKYSPQCKLLIVSNPVDILTYVAWKISGFPKNRVIGSGCNLDS
ARFRYLMGERLGVHPLSCHGWVLGEHGDSSVPVWSGVNVAGVSLKSLNP
QLGTDADKEQWKDVHKQVVDSAYEVIKLKGYTSWAIGLSVADLAESIMK
NLRRVHPISTMIKGLYGIKEDVFLSVPCILGQNGISDVVKVTLTPDEEA
RLKKSADTLWGIQKELQF

FIG. 12B

GAGCAACTTGGCGCTCTACTTGCTGTAGGGCTCTGGGTGATGGGAGAAGAGCGGGAG
GGCAGCTTTCTAACCATATAAGAGGAGATACCATCCCCTTTTGGTTCATCAAG **ATG**A
GTAAGTCCTCAGGCGGCTACACGTACACGGAGACCTCGGTATTATTTTTCCATTTCA
AGGTCTCAAAAGATTCAAAGTCCAAGATGGCAACCCTCAAGGACCAGCTGATTGTGA
ATCTTCTTAAGGAAGAGCAGGCTCCCCAGAACAAGATTACAGTTGTTGGGGTTGGTG
CTGTTGGCATGGCTTGTGCCATCAGTATCTTAATGAAGGACTTGGCGGATGAGCTTG
CCCTTGTTGACGTCATGGAAGACAAACTCAAGGGCGAGATGATGGATCTCCAGCATG
GCAGCCTCTTCCTTAAAACACCAAAAATTGTCTCCAGCAAAGACTACTGTGTAACTG
CGAACTCCAAGCTGGTCATTATCACCGCGGGGGCCCGTCAGCAAGAGGGGGAGAGCC
GGCTCAACCTGGTCCAGCGAAACGTGAACATCTTCAAGTTCATCATTCCCAACATTG
TCAAGTACAGTCCACACTGCAAGCTGCTGATCGTCTCCAATCCAGTGGATATCTTGA
CCTACGTGGCTTGGAAAATCAGTGGCTTTCCCAAAAACCGAGTAATTGGAAGTGGTT
GCAATCTGGATTCAGCGCGGTTCCGTTACCTGATGGGAGAGAGGCTGGGGGTTCACG
CGCTGAGCTGTCACGGCTGGGTCCTGGGAGAACATGGCGACTCCAGTGTGCCTGTGT
GGAGTGGTGTGAATGTTGCCGGCGTCTCCCTGAAGTCTCTTAACCCAGAACTGGGCA
CTGACGCAGACAAGGAGCAGTGGAAGGAGGTTCACAAGCAGGTGGTGGACAGTGCCT
ACGAGGTGATCAAGCTGAAAGGTTACACATCCTGGGCCATTGGCCTCTCTGTGGCAG
ACTTGGCTGAGAGCATAATGAAGAACCTTAGGCGGGTGCATCCCATTTCCACCATGA
TTAAGGGTCTCTATGGAATCAATGAGGATGTCTTCCTCAGTGTCCCATGTATCCTGG
GACAAAATGGAATCTCGGATGTTGTGAAGGTGACACTGACTCCTGAGGAAGAGGCCC
GCCTGAAGAAGAGCGCAGACACCCTCTGGGGAATCCAGAAGGAGCTGCAGTTCTAAA
GTCTTCCCCGTGTCCTAGCACTTCACTGTCCAGGCTGCAGCAGGGCTTCTAGGCAGA
CCACACCCTTCTCGTCTGAGCTGTGGTTAGTACAGTGGTGTTGAGATGGTGTGGGGA
AACATCTCACTCCCCACAGCTCTGCCCTGCTGCCAAGTGGTACTTGTGTAGTGGTGA
CCTGGTTAGTGTGACAGTCCCACTGTCTCTGAGACACACTGCCAACTGCAGGCTTCG
ATTACCCCTGTGAGCCTGCTGCATTGCTGCCCTGCACCAAACAGCCTAGGCCGACGA
GTTCCCAGTTAAGTCGTATAACCTGGCTCCAGTGTGTACGTCCATGATGCATATCTT
GTGCATAAATGTTGTACAGGATATTTTATATATTATATGTGTCTGTAGTGTGCATTG
CAATATTATGTGAGATGTAAGATCTGCATATGGATGATGGAACCAACCACCCAAGTG
TCATGCCAAATAAAACCTTGAACAGTG

FIG. 12C

MSKSSGGYTYTETSVLFFHFKVSKDSKSKMATLKDQLIVNLLKEEQAPQ
NKITVVGVGAVGMACAISILMKDLADELALVDVMEDKLKGEMMDLQHGS
LFLKTPKIVSSKDYCVTANSKLVIITAGARQQEGESRLNLVQRNVNIFK
FIIPNIVKYSPHCKLLIVSNPVDILTYVAWKISGFPKNRVIGSGCNLDS
ARFRYLMGERLGVHALSCHGWVLGEHGDSSVPVWSGVNVAGVSLKSLNP
ELGTDADKEQWKEVHKQVVDSAYEVIKLKGYTSWAIGLSVADLAESIMK
NLRRVHPISTMIKGLYGINEDVFLSVPCILGQNGISDVVKVTLTPEEEA
RLKKSADTLWGIQKELQF

FIG. 12D

CTCTGGTGTTTACTTGAGAAGCCCTGGCTGTGTCCTTGCTGTAGGAGCCGGAGTAG
CTCAGAGTGATCTTGTCTGAGGAAAGGCCAGCCCCACTTGGTTAATAAACCGCGAT
GGGTGAACCCTCAGGAGGCTATACTTACACCCAAACGTCGATATTCCTTTTCCACG
CTAAGATTCCTTTTGGTTCCAAGTCCAATATGGCAACTCTAAAGGATCAGCTGATT
TATAATCTTCTAAAGGAAGAACAGACCCCCCAGAATAAGATTACAGTTGTTGGGGT
TGGTGCTGTTGGCATGGCCTGTGCCATCAGTATCTTAATGAAGGACTTGGCAGATG
AACTTGCTCTTGTTGATGTCATCGAAGACAAATTGAAGGGAGAGATGATGGATCTC
CAACATGGCAGCCTTTTCCTTAGAACACCAAAGATTGTCTCTGGCAAAGACTATAA
TGTAACTGCAAACTCCAAGCTGGTCATTATCACGGCTGGGGCACGTCAGCAAGAGG
GAGAAAGCCGTCTTAATTTGGTCCAGCGTAACGTGAACATATTTAAATTCATCATT
CCTAATGTTGTAAAATACAGCCCGAACTGCAAGTTGCTTATTGTTTCAAATCCAGT
GGATATCTTGACCTACGTGGCTTGGAAGATAAGTGGTTTTCCCAAAAACCGTGTTA
TTGGAAGTGGTTGCAATCTGGATTCAGCCCGATTCCGTTACCTGATGGGGGAAAGG
CTGGGAGTTCACCCATTAAGCTGTCATGGGTGGGTCCTTGGGGAACATGGAGATTC
CAGTGTGCCTGTATGGAGTGGAATGAATGTTGCTGGTGTCTCTCTGAAGACTCTGC
ACCCAGATTTAGGGACTGATAAAGATAAGGAACAGTGGAAAGAGGTTCACAAGCAG
GTGGTTGAGAGTGCTTATGAGGTGATCAAACTCAAAGGCTACACATCCTGGGCTAT
TGGACTCTCTGTAGCAGATTTGGCAGAGAGTATAATGAAGAATCTTAGGCGGGTGC
ACCCAGTTTCCACCATGATTAAGGGTCTTTACGGAATAAAGGATGATGTCTTCCTT
AGTGTTCCTTGCATTTTGGGACAGAATGGAATCTCAGACCTTGTGAAGGTGACTCT
GACTTCTGAGGAAGAGGCCCGTTTGAAGAAGAGTGCAGATACACTTTGGGGGATCC
AAAAGGAGCTGCAATTTTAAAGTCTTCTGATGTCATATCATTTCACTGTCTAGGCT
ACAACAGGATTCTAGGTGGAGGTTGTGCATGTTGTCCTTTTTATCTGATCTGTGAT
TAAAGCAGTAATATTTTAAGATGGACTGGGAAAAACATCAACTCCTGAAGTTAGAA
ATAAGAATGGTTTGTAAAATCCACAGCTATATCCTGATGCTGGATGGTATTAATCT
TGTGTAGTCTTCAACTGGTTAGTGTGAAATAGTTCTGCCACCTCTGACGCACCACT
GCCAATGCTGTACGTACTGCATTTGCCCCTTGAGCCAGGTGGATGTTTACCGTGTG
TTATATAACTTCCTGGCTCCTTCACTGAACATGCCTAGTCCAACATTTTTTCCCAG
TGAGTCACATCCTGGGATCCAGTGTATAAATCCAATATCATGTCTTGTGCATAATT
CTTCCAAAGGATCTTATTTTGTGAACTATATCAGTAGTGTACATTACCATATAATG
TAAAAAGATCTACATACAAACAATGCAACCAACTATCCAAGTGTTATACCAACTAA
AACCCCCAATAAACCTTGAACAGTG

FIG. 12E

MGEPSGGYTYTQTSIFLFHAKIPFGSKSNMATLKDQLIYNLLKEEQTP
QNKITVVGVGAVGMACAISILMKDLADELALVDVIEDKLKGEMMDLQH
GSLFLRTPKIVSGKDYNVTANSKLVIITAGARQQEGESRLNLVQRNVN
IFKFIIPNVVKYSPNCKLLIVSNPVDILTYVAWKISGFPKNRVIGSGC
NLDSARFRYLMGERLGVHPLSCHGWVLGEHGDSSVPVWSGMNVAGVSL
KTLHPDLGTDKDKEQWKEVHKQVVESAYEVIKLKGYTSWAIGLSVADL
AESIMKNLRRVHPVSTMIKGLYGIKDDVFLSVPCILGQNGISDLVKVT
LTSEEEARLKKSADTLWGIQKELQF

FIG. 12F

```
CLUSTALW (V1.4) MULTIPLE SEQUENCE ALIGNMENT

3 SEQUENCES ALIGNED             ALIGNMENT SCORE = 26102
GAPS INSERTED = 78              CONSERVED IDENTITIES = 1013

PAIRWISE ALIGNMENT MODE: SLOW
PAIRWISE ALIGNMENT PARAMETERS:
    OPEN GAP PENALTY = 10.0     EXTEND GAP PENALTY = 5.0

MULTIPLE ALIGNMENT PARAMETERS:
    OPEN GAP PENALTY = 0.0      EXTEND GAP PENALTY = 5.0
    DELAY DIVERGENT = 40%       TRANSITIONS: WEIGHTED

PROCESSING TIME: 8.7 SECONDS

RAT     1           CGCTC-TACTTGCTGT-AGGA-CTCTGG--GTGA--TGG  32
HUM     1           CTCTGGTGTTTACT-TGAGAAGCCCTGGCTGTGTCCTTG  38
MOU     1 GAGCAACTTGGCGCTC-TACTTGCTGT-AGGG-CTCTGG--GTGA--TGG  43
                    * **  *  ** ** * **   * ****  ***   * *

RAT    33 GAG-AAGAGCGGGAGGGCAGTTCTT--TAACCGTGTAAGAGGAGGGACCA  79
HUM    39 CTGTAGGAGCCGGA--GTAGCTCAGAGTGATCTTGTCTGAGGAAAGGCCA  86
MOU    44 GAG-AAGAGCGGGAGGGCAGCTTTC--TAACCATATAAGAGGAGATACCA  90
            * * **** ***  * ** *     * * * * * *****    ***

RAT    80 TCCCT-TTTGG--GGTTCATCAAGATGAGTAAGAACTCAGGCGGCTACAC 126
HUM    87 GCCCCACTTGGTTAATAAACCGCGATGGGTGAACCCTCAGGAGGCTATAC 136
MOU    91 TCCCC-TTTTG--G-TTCATCAAGATGAGTAAGTCCTCAGGCGGCTACAC 136
           ***   ** *    *  * *  **** ** *   ****** ***** **

RAT   127 ATATACGGAGACCTCAGTATTATTTTTCCATTTCAAGGTCCCAAAAGATT 176
HUM   137 TTACACCCAAACGTCGATATTCCTTTTCCACGCTAAGATTCCTTTTGGTT 186
MOU   137 GTACACGGAGACCTCGGTATTATTTTTCCATTTCAAGGTCTCAAAAGATT 186
           ** **  * ** **  ****  *******    *** *  *    * **

RAT   177 CAAAGTCCAAGATGGCAGCCCTCAAGGACCAGCTGATT-GTGAATCTTCT 225
HUM   187 CCAAGTCCAATATGGCAACTCTAAAGGATCAGCTGATTTAT-AATCTTCT 235
MOU   187 CAAAGTCCAAGATGGCAACCCTCAAGGACCAGCTGATT-GTGAATCTTCT 235
          * ******** ****** * ** ***** *********   * ********

RAT   226 TAAGGAAGAACAGGTCCCCCAGAACAAGATTACAGTTGTTGGGGTTGGTG 275
HUM   236 AAAGGAAGAACAGACCCCCCAGAATAAGATTACAGTTGTTGGGGTTGGTG 285
MOU   236 TAAGGAAGAGCAGGCTCCCCAGAACAAGATTACAGTTGTTGGGGTTGGTG 285
           ******** ***   ******** ************************

RAT   276 CTGTTGGCATGGCTTGTGCCATCAGTATCTTAATGAAGGACTTGGCTGAT 325
HUM   286 CTGTTGGCATGGCCTGTGCCATCAGTATCTTAATGAAGGACTTGGCAGAT 335
MOU   286 CTGTTGGCATGGCTTGTGCCATCAGTATCTTAATGAAGGACTTGGCGGAT 335
          ************* ******************************** ***
```

FIG. 13A

```
RAT  326 GAGCTTGCCCTTGTTGATGTCATAGAAGATAAGCTAAAGGGAGAGATGAT 375
HUM  336 GAACTTGCTCTTGTTGATGTCATCGAAGACAAATTGAAGGGAGAGATGAT 385
MOU  336 GAGCTTGCCCTTGTTGACGTCATGGAAGACAAACTCAAGGGCGAGATGAT 385
         ** ***** ******** ***** ***** **  * ***** ********

RAT  376 GGATCTTCAGCATGGCAGCCTTTTCCTTAAGACACCAAAAATTGTCTCCA 425
HUM  386 GGATCTCCAACATGGCAGCCTTTTCCTTAGAACACCAAAGATTGTCTCTG 435
MOU  386 GGATCTCCAGCATGGCAGCCTCTTCCTTAAAACACCAAAAATTGTCTCCA 435
         ****** ** *********** *******  ******** ********

RAT  426 GCAAAGATTATAGTGTGACTGCAAACTCCAAGCTGGTCATTATCACCGCG 475
HUM  436 GCAAAGACTATAATGTAACTGCAAACTCCAAGCTGGTCATTATCACGGCT 485
MOU  436 GCAAAGACTACTGTGTAACTGCGAACTCCAAGCTGGTCATTATCACCGCG 485
         ******* **   *** ***** *********************** **

RAT  476 GGGGCCCGTCAGCAAGAGGGAGAGAGCCGGCTCAATTTGGTCCAGCGAAA 525
HUM  486 GGGGCACGTCAGCAAGAGGGAGAAAGCCGTCTTAATTTGGTCCAGCGTAA 535
MOU  486 GGGGCCCGTCAGCAAGAGGGGGAGAGCCGGCTCAACCTGGTCCAGCGAAA 535
         ***** ************** ** ***** ** **  ********** **

RAT  526 CGTGAACATCTTCAAGTTCATCATTCCAAATGTTGTGAAATACAGTCCAC 575
HUM  536 CGTGAACATATTTAAATTCATCATTCCTAATGTTGTAAAATACAGCCCGA 585
MOU  536 CGTGAACATCTTCAAGTTCATCATTCCCAACATTGTCAAGTACAGTCCAC 585
         ********* ** ** *********** **  **** ** ***** **

RAT  576 AGTGCAAACTGCTCATCGTCTCAAACCCAGTGGATATCTTGACCTACGTG 625
HUM  586 ACTGCAAGTTGCTTATTGTTTCAAATCCAGTGGATATCTTGACCTACGTG 635
MOU  586 ACTGCAAGCTGCTGATCGTCTCCAATCCAGTGGATATCTTGACCTACGTG 635
         * *****  **** ** ** ** ** ************************

RAT  626 GCTTGGAAGATCAGCGGCTTCCCCAAAAACAAAGTTATTGGAAGTGGTTG 675
HUM  636 GCTTGGAAGATAAGTGGTTTTCCCAAAAACCGTGTTATTGGAAGTGGTTG 685
MOU  636 GCTTGGAAAATCAGTGGCTTTCCCAAAAACCGAGTAATTGGAAGTGGTTG 685
         ******** ** ** ** ** *********   ** **************

RAT  676 CAATCTGGATTCGGCTCGGTTCCGTTACCTGATGGGAGAAAGGCTGGGAG 725
HUM  686 CAATCTGGATTCAGCCCGATTCCGTTACCTGATGGGGGAAAGGCTGGGAG 735
MOU  686 CAATCTGGATTCAGCGCGGTTCCGTTACCTGATGGGAGAGAGGCTGGGGG 735
         ************ ** ** ***************** ** ******** *

RAT  726 TTCATCCACTGAGCTGTCACGGGTGGGTCCTGGGAGAGCATGGCGACTCC 775
HUM  736 TTCACCCATTAAGCTGTCATGGGTGGGTCCTTGGGGAACATGGAGATTCC 785
MOU  736 TTCACGCGCTGAGCTGTCACGGCTGGGTCCTGGGAGAACATGGCGACTCC 785
         ****  *  * ******** ** ******** ** ** ***** ** ***

RAT  776 AGTGTGCCTGTGTGGAGTGGTGTGAACGTCGCCGGCGTCTCCCTGAAGTC 825
HUM  786 AGTGTGCCTGTATGGAGTGGAATGAATGTTGCTGGTGTCTCTCTGAAGAC 835
MOU  786 AGTGTGCCTGTGTGGAGTGGTGTGAATGTTGCCGGCGTCTCCCTGAAGTC 835
         *********** ********  **** ** ** ** ***** ****** *
```

FIG. 13B

```
RAT  826 TCTGAACCCGCAGCTGGGCACGGATGCAGACAAGGAGCAGTGGAAGGATG  875
HUM  836 TCTGCACCCAGATTTAGGGACTGATAAAGATAAGGAACAGTGGAAAGAGG  885
MOU  836 TCTTAACCCAGAACTGGGCACTGACGCAGACAAGGAGCAGTGGAAGGAGG  885
         ***  ****  *  * ** ** **   *** ***** ******** ** *

RAT  876 TGCACAAGCAGGTGGTTGACAGTGCATACGAAGTGATCAAGCTGAAAGGT  925
HUM  886 TTCACAAGCAGGTGGTTGAGAGTGCTTATGAGGTGATCAAACTCAAAGGC  935
MOU  886 TTCACAAGCAGGTGGTGGACAGTGCCTACGAGGTGATCAAGCTGAAAGGT  935
         * ************** ** ***** ** ** ******** ** *****

RAT  926 TACACATCCTGGGCCATTGGCCTCTCCGTGGCAGACTTGGCCGAGAGCAT  975
HUM  936 TACACATCCTGGGCTATTGGACTCTCTGTAGCAGATTTGGCAGAGAGTAT  985
MOU  936 TACACATCCTGGGCCATTGGCCTCTCTGTGGCAGACTTGGCTGAGAGCAT  985
         ************** ***** ***** ** ***** ***** ***** **

RAT  976 AATGAAGAACCTTAGGCGGGTGCATCCCA-TTTCCACCATGATTAAGGGT 1024
HUM  986 AATGAAGAATCTTAGGCGGGTGCA-CCCAGTTTCCACCATGATTAAGGGT 1034
MOU  986 AATGAAGAACCTTAGGCGGGTGCATCCCA-TTTCCACCATGATTAAGGGT 1034
         ********* ************** **** ********************

RAT 1025 CTCTATGGGATCAAGGAGGATGTCTTCCTCAGCGTCCCATGTATCCTGGG 1074
HUM 1035 CTTTACGGAATAAAGGATGATGTCTTCCTTAGTGTTCCTTGCATTTTGGG 1084
MOU 1035 CTCTATGGAATCAATGAGGATGTCTTCCTCAGTGTCCCATGTATCCTGGG 1084
         ** ** ** ** ** ** *********** ** ** ** ** **  ****

RAT 1075 ACAAAATGGAATCTCAGATGTTGTGAAGGTGACACTGACTCCTGACGAGG 1124
HUM 1085 ACAGAATGGAATCTCAGACCTTGTGAAGGTGACTCTGACTTCTGAGGAAG 1134
MOU 1085 ACAAAATGGAATCTCGGATGTTGTGAAGGTGACACTGACTCCTGAGGAAG 1134
         *** *********** **  ************* ****** **** ** *

RAT 1125 AGGCCCGCCTGAAGAAGAGTGCAGATACCCTCTGGGGAATCCAGAAGGAG 1174
HUM 1135 AGGCCCGTTTGAAGAAGAGTGCAGATACACTTTGGGGGATCCAAAAGGAG 1184
MOU 1135 AGGCCCGCCTGAAGAAGAGCGCAGACACCCTCTGGGGAATCCAGAAGGAG 1184
         *******  ********** ***** ** ** ***** ***** ******

RAT 1175 CTGCAGTTCTAAAGTCTTCCCAGTGTCCTAGCACTTCACTGTCCAGGCTG 1224
HUM 1185 CTGCAATTTTAAAGTCTTCT-GATGTCATATCATTTCACTGTCTAGGCTA 1233
MOU 1185 CTGCAGTTCTAAAGTCTTCCCCGTGTCCTAGCACTTCACTGTCCAGGCTG 1234
         ***** ** **********    **** ** ** ********* *****

RAT 1225 CAGCAGGGTTTCTA--TGG-AGACCACGCAC-TT--C-TC---ATCTGAG 1264
HUM 1234 CAACAGGATT-CTAGGTGG-AGGTTGTGCATGTTGTCCTTTTTATCTGAT 1281
MOU 1235 CAGCAGGGCTTCTA---GGCAGACCACACCC-TT--C-TC---GTCTGAG 1274
         ** ****  * ***   ** **      *   **  * *     *****

RAT 1265 CTGTGGTTAGTCCAGTTG-GTCCAAAG                        1290
HUM 1282 CTGTGATTAAAGCAGTAATATTTTAAGATGGACTGGAAAAACATCAACT 1331
MOU 1275 CTGTGGTTAGTACAGT-G-GTGTTGAGATGGTGTGGGGAAA-CAT---CT 1318
         ***** ***   ****    *    **
```

FIG. 13C

```
RAT 1291                                                    1290
HUM 1332 CCTGAAGTTAGAAATAAGAATGGTTTGTAAAATCCACAGCTATATCCTGA 1381
MOU 1319 C---A--CT-----C-----------------CCCACAGCTCTGCCCTGC 1341

RAT 1291                                                    1290
HUM 1382 TGCTGGATGGTATTAATCTTGTGTAGTCTTCAACTGGTTAGTGTGAAATA 1431
MOU 1342 TGCCAAGTGG---TA--CTTGTGTAGTGGTGACCTGGTTAGTGTGA--CA 1384

RAT 1291                                                    1290
HUM 1432 GTTCTGCCACCTCTGACGCACCACTGCCAATGCTGTACGTACTGCATTTG 1481
MOU 1385 GTCCCACTGTCTCTGAGACAC-ACTGCCAA--CTGCA-G-GCTTCGATTA 1429

RAT 1291                                                    1290
HUM 1482 CCCCTTGAGCCAGGTGGATGTTTACCGTGTGTTATATAACTTCCTGGCTC 1531
MOU 1430 CCCCT-------G-TG-A-G----CC-TG--CTG--C-A-TTGCTG-C-C 1456

RAT 1291                                                    1290
HUM 1532 CTTCACTGAACATGCCTAGTCCAACATTTTTTCCCAGT-GAGTCACATC- 1579
MOU 1457 CTGCACCAAACA-GCCTAGGCCGACGAGTT--CCCAGTTAAGTCGTATAA 1503

RAT 1291                                                    1290
HUM 1580 CTGGGATCCAGTGTATAAATCCAATAT-CATGTCTTGTGCATAATTCTTC 1628
MOU 1504 CCTGGCTCCAGTGTGTACGTCCATGATGCATATCTTGTGCATAAATGTTG 1553

RAT 1291                                                    1290
HUM 1629 CAAAGGATCTTATTT-TGTGAACTATATCAGTAGTGTACATTACCATATA 1677
MOU 1554 TACAGGATATTTTATATATTATATGTGTCTGTAGTGTGCATTGCAATATT 1603

RAT 1291                                                    1290
HUM 1678 ATGTAA-A---AAGATCTACATACAAACAATGCAACCAACTATCCAAGTG 1723
MOU 1604 ATGTGAGATGTAAGATCTGCATATGGATGATGGAACCAACCACCCAAGTG 1653

RAT 1291                                      1290
HUM 1724 TTATACCAACTAAAACCCCCAATAA-ACCTTGAACAGTG 1761
MOU 1654 TCATGCCAAATAAAACCTTGAACAGTG            1680
```

FIG. 13D

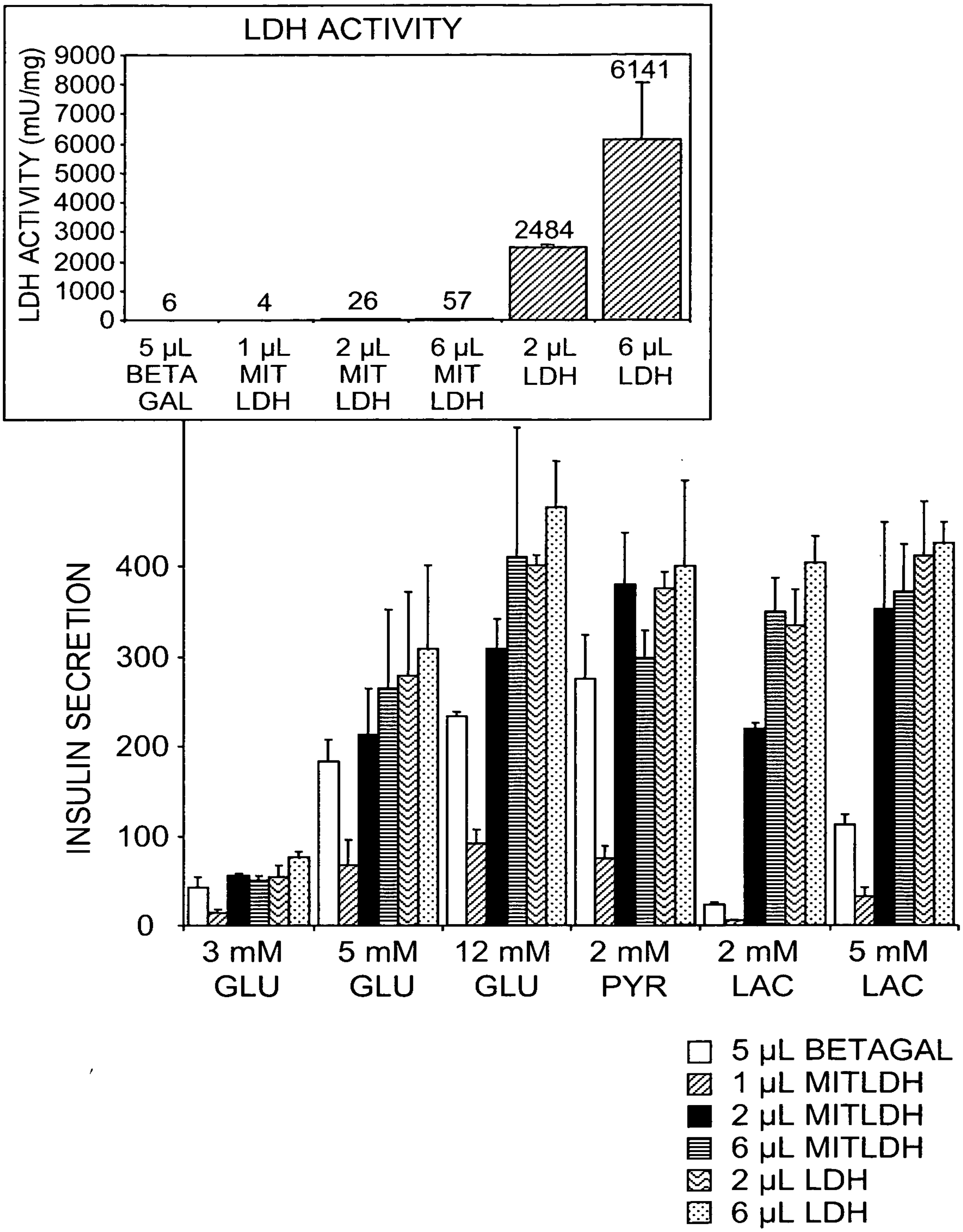

LDH ACTIVITY
LDH ACTIVITY (mU/mg)
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
6
4
26
57
2484
6141
5 μL BETA GAL
1 μL MIT LDH
2 μL MIT LDH
6 μL MIT LDH
2 μL LDH
6 μL LDH
INSULIN SECRETION
400
300
200
100
0
3 mM GLU
5 mM GLU
12 mM GLU
2 mM PYR
2 mM LAC
5 mM LAC
5 μL BETAGAL
1 μL MITLDH
2 μL MITLDH
6 μL MITLDH
2 μL LDH
6 μL LDH

FIG. 14